withdrawal of Claims 7, 8, 11-18, 22 and 23 from consideration by Examiner Davenport pursuant to restriction requirement.

Applicants respectfully traverse the instant restriction requirement on the following grounds. Claims 7, 8, 11-14, 22 and 23 (designated Group II), being drawn to a radiolabeled complex, are believed sufficiently related to the elected claims (Group I) that is is believed not to be an undue burden for these claims to be searched and examined together. Similarly, claim 18, drawn to a specific composition of matter comprising one specific embodiment of generic claim 1, is believed amenable to concurrent search and examination without undue burden on Patent Office resources. This is evidenced by the classification of the claims of Group I and Group V in the same class (530) and related subclasses (330 and 335, respectively).

Applicants respectfully request Examiner Davenport to reconsider the restriction requirement as to Groups II and V and to examine claims 7, 8, 11-14, 18, 22 and 23 along with the elected claims, to expedite prosecution of the application and avoid undue cost and delay on the part of Applicants.

2. <u>The Claims are fully enabled by the specification</u>

The pending claims are rejected on 35 U.S.C. §112, first paragraph grounds, on the asserted basis that the specification does not enable claims having their scope. Applicants respectfully traverse with the following argument.

Preliminarily, Applicant wishes to note that the Official Action cites the case of *In re Fisher* in support of the proposition that "[p]eptides are well known...to be

unpredictable." Insofar as the nonenablement argument in the Official Action is asserted to be supported by the *Fisher* case, Applicant draws the following distinctions. The first is that the *Fisher* case is twenty-five years old, and the factual basis for any statements in *Fisher* on predictability in the peptide arts should be given no evidentiary weight. Further, the claimed peptide compositions at issue in the *Fisher* case were admittedly *im*pure biological isolates of the hormone ACTH, claimed as having utility in the alleviation of a variety of ACTH-related diseases and maladies. On those facts, the Patent Office (and the CCPA) cast a skeptical eye on the broad scope of the invention claimed. Moreover, the only functional limitation present in the Fischer application related to an activity that was at least 1 International Unit. The court specifically noted the broad scope of a composition having such a minimal activity limitation, with no upper limit, and the adverse public policy consequences of allowing an admittedly *im*pure preparation having low specific activity to inhibit the development of better, *more* pure, *more* active ACTH preparations.

In contrast, the present inventor has taught that the only reagents falling within the scope of his patent claims are those comprising (a) a specific binding compound that is less than 10,000 daltons in molecular weight and (b) that specifically binds to a target site to be imaged, covalently linked to (d) a radiolabel complexing moiety, wherein the reagents of the invention (e) are useful for preparing a scintigraphic imaging agent for imaging target sites within a mammalian body. Applicant respectfully contends that the teachings of the *Fisher* case are inapposite to his invention, in general because of the admitted advances in the small-molecule

pharmaceutical arts over the past twenty-five years, and specifically, because he has crafted his claim language to exactly inform the future on the structural and functional characteristics of the reagents that fall within the scope of his claims. Applicant respectfully contends that, whatever *Fisher* stands for, it does not stand for the proposition that the instant case is in any way analogous to the *Fisher* teachings.

The Official Action points out four asserted deficiencies in the specification and claims:

1. that the scope of the claims are not supported by the specification, particularly because there is assertedly no guidance as to which of the large number of specific binding compounds that can be envisioned will fall within the claims; and

2. that amino acids other than cysteine have not been exemplified for the claimed radiolabel complexing moieties; and

3. that the linker may impact the binding activity of the specific binding peptide; and

4. that the practice of the claimed invention would constitute undue experimentation.

Applicant contends that one having ordinary skill in the art was in possession of the knowledge of what a "specific binding compound" comprised at the time the invention was made. As evidence of this fact, Applicant has directed the performance of a computer database search of the scientific literature for the descriptors "specific binding" with "peptide". This search uncovered 1413 references from 1966 to date; then the search field was limited to the twenty-five years prior to the filing date of the

instant application (1966-1990) almost 800 references were found. Applicant has appended a paper copy of a portion of this search as Exhibit A, consisting of the 50 chronologically most recent references. Applicant respectfully contends that these results show that one of ordinary skill in the art would have understood the meaning of the term "specific binding compound." Moreover, the skilled worker would have been able to identify any particular one among a plethora of specific binding compounds, including peptides, which Applicant contends his specification enables one of ordinary skill to combine with the disclosed Tc-99m chelating moiety to produce a reagent of the invention to preparing a scintigraphic imaging agent. Applicant respectfully contends that this is all he is required to do to fulfill the requirements of 35 U.S.C. §112, first paragraph.

Applicant further notes that his claims carry a number of significant limitations on the identity of the specific binding compounds that fall within their scope. Such specific binding compounds must first be capable of being used to prepare a scintigraphic imaging agent for imaging sites in a mammalian body. Such compounds must specifically bind to a component found at target site to be imaged. As described above, identification of such specific binding compounds, including, for example, peptides, was well within the ability of one of ordinary skill in the art. In addition, the specific binding compound comprising the reagent must have a molecular weight of less than 10,000 daltons to fall within the scope of the claims. These limitations, which comprise both functional and structural limitations, define the scope of the specific binding compounds encompassed by the claims. The simple fact is that the

number of compounds that satisfy these criteria is far smaller than the total number of compounds having a molecular weight less than 10,000 daltons that can be envisioned. The only way to contend that the two sets of compounds have a similar extent is to *ignore* all of the limitations *other than* the size limitation. However, the patent law requires that all the limitations in a claim be considered, as a whole, in determining the propriety of the metes and bounds of the claim. Applicant respectfully submits that the pending claims fulfill the enablement requirement of §112, because the ordinarily skilled person would understand the limited subset of specific binding compounds that fall within its scope.

Applicant further contends that teachings in the specification sufficient to enable the person of ordinary skill to practice his invention can be found on pages 12 and 19, where a number of exemplary reagents are disclosed. Applicant respectfully submits that the scope and breadth of these teachings, in view of the understanding of the art by the worker of ordinary skill, enable the ordinarily-skilled individual to make and use the specific binding compound-containing reagents that fall within the ambit of the claimed invention.

Regarding the second assertion made in the Official Action, the radiolabel complexing moieties of the invention have been exemplified in the specification by particular embodiments comprising cysteine as the sulfur-containing component of this moiety. In addition, contrary to the assertion in the Official Action that only cysteine has been explicitly exemplified, Applicants respectfully direct the Examiner's attention to Example 5, wherein a radiolabel complexing moiety comprising mercaptoacetic acid

is explicitly disclosed (see p.23, line 3). It is well-established patent law that claims are not limited solely to what is explicitly disclosed by example. Were it to be otherwise, patent specifications would contain vast quantities of exemplified compounds, far in excess of that required to inform the skilled man how to make and use the invention, and causing a burden on both the Patent Office during prosecution and to the public upon expiration of the patent term, as the critical features of the invention would be masked by excessive and unnecessary disclosure. Rather, a patent application must only provide sufficient examples and written description to put the man of ordinary skill in possession of his invention. Applicant respectfully contends that the instant specification fulfills this requirement regarding the radiolabel complexing moiety.

In support of this argument, Applicant provides herewith (as Exhibits B through M) a series of chemical structure drawings showing the radiochemical chelation complex of Tc-99m with radiolabel complexing moieties of the invention comprising each of the thiol-containing components of said moieties (*specifically*, cysteine, mercaptoacetic acid, mercaptopropionic acid, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine and 3-mercaptopropylamine). Applicant respectfully contends that, *having been given the explicit teachings of the instant specification exemplifying embodiments of such radiolabel chelating moieties comprising cysteine and mercaptoacetic acid*, one of ordinary skill in the art would have appreciated the use of the chemically-equivalent thiol-containing species (homocysteine, isocysteine, penicillamine, mercaptopropionic acid, 2-mercaptoethylamine and 3-

thiol containing - ok'd if limited to that.

mercaptopropylamine) in embodiments such as those shown in the accompanying Exhibits. Further, the skilled worker, armed with the instant inventors' teachings, would have understood the metes and bounds of the invention and would have been able to practice the invention throughout the claimed range without undue experimentation. With regard to the chemical identities of amino acids 1 and 2, moreover, the chemical structures illustrate that the sidechains of the amino acids in this position have *no* effect or influence on the structure or radiochemical function of the radiolabel chelating moiety, *provided* the amino acid is a primary α- or β-amino acid that does not contain a thiol group. Applicant therefore respectfully contends that the claims are enabled throughout the range of the recited species, and fulfill the requirements of 35 U.S.C. §112.

Thirdly, the Official Action raises the issue of whether the linker moiety affects the biological activity of the reagent. Applicant respectfully contends that, as disclosed in the specification, the linker moiety is designed as a chemically inert spacer between the two functional components of the reagents of the invention: a specific binding compound, and a radiolabel chelating moiety. These two elements are covalently linked together. However, operative embodiments of the reagents of the invention, as disclosed in the specification, also can contain a linking moiety, comprising an amino acid or a peptide. Thus, one of ordinary skill would understand that the peptide linker is limited to such functionally inert embodiments, and chosen specifically *not* to interfere with the biological activity (*i.e.*, *either* specific binding *or* radiolabel chelating) of the functional components of the reagents of the invention.

Applicant respectfully contends that such inert linker moieties are well understood in the chemical and pharmaceutical arts, and absent evidence to the contrary believes that one or ordinary skill would have been able to practice the claimed invention without undue experimentation.

Applicant respectfully submits that the claims are enabled because the skilled worker would understand from the instant specification how to make and use the claimed invention without undue experimentation. Applicant respectfully submits that if the worker of ordinary skill has enough skill to establish the identity of a specific binding compound in the first place, such a worker will have sufficient skill to make and use the invention as taught in the instant specification. How to use the invention is explicitly described in the specification, *inter alia* on page 8.

For all of the above reasons, Applicant respectfully contends that the outstanding rejections based on 35 U.S.C. §112, first paragraph have been overcome by amendment or traversed by argument, and respectfully request that these rejections be withdrawn

Applicant believes that all the requirements of 35 U.S.C. §112 have been met, and respectfully requests that the outstanding rejections be withdrawn.

CONCLUSIONS

It is believed that all 35 U.S.C. §112 requirements are fully met, and allowance of the claims is respectfully solicited.

Respectfully submitted,
BANNER & ALLEGRETTI, Ltd.

By _____
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